FILE 'REGISTRY' ENTERED AT 15:18:59 ON 06 DEC 2002
L1 42 SEA ABB=ON PLU=ON NANPNVDPNANPNANP|IEYLNKIQNSLSTEWS
PCSVT|EYLNKIQNSLSTEWSPCSVT/SQSP

FILE 'HCAPLUS' ENTERED AT 15:21:50 ON 06 DEC 2002

L2 30 SEA ABB=ON PLU=ON L1

L3 22 SEA ABB=ON PLU=ON L2 AND MALARIA#

L3 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2002:752116 HCAPLUS 137:289735

DOCUMENT NUMBER: TITLE:

Sequence of Plasmodium falciparum chromosomes 1,

3-9 and 13

AUTHOR(S):

Hall, N.; Pain, A.; Berriman, M.; Churcher, C.;
Harris, B.; Harris, D.; Mungall, K.; Bowman, S.;
Atkin, R.; Baker, S.; Barron, A.; Brooks, K.;
Buckee, C. O.; Burrows, C.; Cherevach, I.;

Chillingworth, C.; Chillingworth, T.; Christodoulou, Z.; Clark, L.; Clark, R.; Corton, C.; Cronin, A.; Davies, R.; Davis, P.; Dear, P.; Dearden, F.; Doggett, J.; Feltwell, T.; Goble, A.; Goodhead, I.; Gwilliam, R.; Hamlin, N.; Hance, Z.; Harper, D.; Hauser, H.; Hornsby, T.; Holroyd, S.; Horrocks, P.; Humphray, S.; Jagels, K.; James, K. D.; Johnson, D.; Kerhornou, A.; Knights, A.; Konfortov, B.; Kyes, S.; Larke, N.; Lawson, D.; Lennard, N.; Line, A.; Maddison, M.; McLean, J.; Mooney, P.; Moule, S.; Murphy, L.; Oliver, K.; Ormond, D.; Price, C.; Quail, M. A.; Rabbinowitsch, E.; Rajandream, M.-A.; Rutter, S.; Rutherford, K. M.; Sanders, M.; Simmonds, M.; Seeger, K.; Sharp, S.; Smith, R.; Squares, R.; Squares, S.; Stevens, K.; Taylor, K.; Tivey, A.; Unwin, L.; Whitehead, S.; Woodward, J.; Sulston, J. E.; Craig, A.; Newbold, C.; Barrell,

B. G.

CORPORATE SOURCE:

The Wellcome Trust Sanger Institute, Hinxton,

Cambridge, CB10 1SA, UK

SOURCE:

Nature (London, United Kingdom) (2002),

419(6906), 527-531

CODEN: NATUAS; ISSN: 0028-0836

Nature Publishing Group

PUBLISHER:
DOCUMENT TYPE:
LANGUAGE:

counterparts.

Journal English

AB Since the sequencing of the first two chromosomes of the malaria parasite, Plasmodium falciparum, there has been a concerted effort to sequence and assemble the entire genome of this organism. This report provides the sequence of chromosomes 1, 3-9 and 13 of P. falciparum clone 3D7; these chromosomes account for apprx.55% of the total genome. The methods used to map, sequence and annotate these chromosomes is described. By comparing these assemblies with the optical map, the completeness of the resulting sequence is indicated. During annotation, Gene Ontol. terms were assigned to the predicted gene products, and clustering of some malaria-specific terms to specific chromosomes was obsd. A highly conserved sequence element was found in the intergenic region of internal var genes that is not assocd. with their telomeric

467522-97-0 TΤ RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (amino acid sequence; sequence of Plasmodium falciparum chromosomes 1, 3-9 and 13) THERE ARE 33 CITED REFERENCES AVAILABLE 33 REFERENCE COUNT: FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2002 ACS L3 2002:142851 HCAPLUS ACCESSION NUMBER: 136:215388 DOCUMENT NUMBER: Immunogenic hepatitis B nucleocapsid protein TITLE: (HBc) chimeric particles having enhanced stability Birkett, Ashley J. INVENTOR(S): PATENT ASSIGNEE(S): Apovia, Inc., USA PCT Int. Appl., 290 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent English . LANGUAGE: FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE -,-----\_\_\_\_\_ \_\_\_\_\_ \_\_\_\_ A2 20020221 WO 2001-US41759 20010816 WO 2002014478 W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 20020225 AU 2001-85452 20010816 AU 2001085452 Α5 US 2000-225843P P 20000816 PRIORITY APPLN. INFO.: US 2000-226867P P 20000822 US 2001-930915 A 20010815 WO 2001-US41759 W 20010816 A chimeric, carboxy-terminal truncated hepatitis B virus AΒ nucleocapsid protein (core protein or HBC) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The immunogenic epitope is a B cell epitope or T cell epitope derived from pathogen such as Streptococcus pneumonia, Cryptosporidium parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestia, etc. The display of the immunogenic epitope is displayed in the immunogenic loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed. ΙT 401552-42-9P RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (amino acid sequence; chimeric proteins comprising HBcAg and T

and/or B cell epitope for use as vaccines)

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151113-09-6 401460-26-2 401460-27-3
IT
     401460-29-5 401460-48-8 401460-49-9
     401460-60-4 401461-03-8
     RL: BSU (Biological study, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (chimeric proteins comprising HBcAg and T and/or B cell epitope
        for use as vaccines)
IT
     401556-50-1
     RL: PRP (Properties)
        (unclaimed nucleotide sequence; immunogenic hepatitis B
        nucleocapsid protein (HBc) chimeric particles having enhanced
        stability)
     401556-53-4
IT
     RL: PRP (Properties)
        (unclaimed protein sequence; immunogenic hepatitis B nucleocapsid
        protein (HBc) chimeric particles having enhanced stability)
    ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS
                         2002:142465 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         136:198912
                        Malaria vaccines comprise Plasmodium
TITLE:
                         CS protein and truncated hepatitis B virus
                         nucleocapsid protein or HBcAg
                         Birkett, Ashley J.
INVENTOR(S):
PATENT ASSIGNEE(S):
                         Apovia, Inc., USA
                         PCT Int. Appl., 197 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                     KIND DATE
                                          APPLICATION NO. DATE
     PATENT NO.
                                           _____
                      ____
                           _____
     WO 2002013765
                      A2
                            20020221
                                           WO 2001-US25625 20010816
            AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ,
            DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC,
            LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG,
             SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
                                           AU 2001-84967
     AU 2001084967
                      Α5
                            20020225
                                                            20010816
PRIORITY APPLN. INFO.:
                                        US 2000-225813P P
                                                            20000816
                                        US 2001-931325
                                                        A 20010815
                                        WO 2001-US25625 W 20010816
    A chimeric, carboxy-terminal truncated hepatitis B virus
AB
     nucleocapsid protein (HBc) is disclosed that contains an immunogen
     for inducing the prodn. of antibodies to malarial
     proteins. An immunogenic malarial epitope is expressed
    between residues 78 and 79 of the HBc immunogenic loop sequence.
     The chimer preferably contains a malaria-specific T cell
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Searcher: Shears 308-4994

epitope and is preferably engineered for both enhanced stability of

self-assembled particles and enhanced yield of those chimeric particles. Methods of making and using the chimers are also disclosed.

IT 151113-09-6 401460-26-2 401460-27-3

401460-29-5 401460-45-5

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antimalarial vaccines comprise Plasmodium CS protein and

truncated hepatitis B virus nucleocapsid protein or HBcAg)

IT 401460-48-8 401460-49-9 401460-60-4 401461-03-8

RL: PRP (Properties)

(unclaimed sequence; malaria vaccines comprise Plasmodium CS protein and truncated hepatitis B virus nucleocapsid protein or HBcAg)

L3 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:900440 HCAPLUS

ACCESSION NUMBER: 2001:9004
DOCUMENT NUMBER: 137:92286

TITLE: Conversion of poorly immunogenic malaria

repeat sequences into a highly immunogenic

vaccine candidate

AUTHOR(S): Milich, David R.; Hughes, Janice; Jones, Joyce;

Sallberg, Matti; Phillips, Tom R.

CORPORATE SOURCE: Vaccine Research Institute of San Diego (VRISD),

San Diego, CA, 92121, USA

SOURCE: Vaccine (2001), 20(5-6), 771-788

CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

The recent success of a Plasmodium falciparum malaria vaccine consisting of circumsporozoite protein (CSP) T and B cell epitopes has rekindled interest in the development of a pre-erythrocytic vaccine. In order to optimize immunogenicity, well-characterized CSP-specific neutralizing B cell epitopes and a universal T cell epitope were combined with an efficient and flexible particulate carrier platform, the hepatitis B core antigen (HBcAg), to produce a novel pre-erythrocytic vaccine candidate. The vaccine candidate, V12.PF3.1, is a potent immunogen in mice eliciting unprecedented levels (greater than 106 titers) of sporozoite-binding antibodies after only two doses. The anti-sporozoite antibodies are long lasting, represent all IgG isotypes, and antibody prodn. is not genetically restricted. CSP-specific CD4+ T cells are also primed by V12.PF3.1 immunization in a majority of murine strains. Furthermore, the hybrid HBcAg-CS particles can be produced inexpensively in bacterial expression systems. These and other characteristics suggest that V12.PF3.1 represents an efficient and economical P. falciparum vaccine candidate for use sep. or in combination with other formulations.

IT 401460-27-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (immunogenic malaria repeat sequences combined with

HBcAg in development of highly immunogenic vaccine)

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L3 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:647507 HCAPLUS

DOCUMENT NUMBER: 136:289638

TITLE: Molecular cloning and sequencing of the

circumsporozoite protein gene from Plasmodium falciparum strain FCC-1/HN and expression of the

gene in mycobacteria

AUTHOR(S): Zheng, Chunfu; Xie, Peimei; Chen, Yatang

CORPORATE SOURCE: Institute of Infectious and Parasitic Diseases,

The First Affiliated Hospital of Chongqing Medical University, Chungking, 400016, Peop.

Rep. China

SOURCE: Journal of Clinical Microbiology (2001), 39(8),

2911-2915

CODEN: JCMIDW; ISSN: 0095-1137
American Society for Microbiology

PUBLISHER: American
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mycobacterium bovis bacillus Calmette-Guerin (BCG) has been used as a live bacterial vaccine to immunize more than 2 billion people against tuberculosis. In an attempt to use this vaccine strain as a vehicle for protective antigens, the Plasmodium falciparum gene from strain FCC-1/HN encoding circumsporozoite protein (CSP) was amplified from the P. falciparum genome, sequenced, and expressed in M. bovis BCG under the control of an expression cassette carrying the promoter of heat shock protein 70 (HSP70) from Mycobacterium tuberculosis. The recombinant shuttle plasmid pBCG/CSP was

tuberculosis. The recombinant shuttle plasmid pBCG/CSP was introduced into mycobacteria by electroporation, and the recombinant mycobacteria harboring pBCG/CSP could be induced by heating to express CSP; the mol. mass of recombinant CSP was about 42 kDa. This report of expression of the almost-full-length P. falciparum CSP gene in BCG provides scientific evidence for the application of the HSP70 promoter in expressing a foreign gene in BCG and in development of BCG as a multivalent vectoral vaccine for

malaria. IT 407646-80-4

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(amino acid sequence; mol. cloning and sequencing of the circumsporozoite protein gene from Plasmodium falciparum strain FCC-1/HN and expression of the gene in mycobacteria)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

L3 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:26336 HCAPLUS

DOCUMENT NUMBER: 134:221126

TITLE: A totally synthetic polyoxime malaria

vaccine containing Plasmodium falciparum B cell and universal T cell epitopes elicits immune responses in volunteers of diverse HLA types Nardin, Elizabeth H.; Calvo-Calle, J. Mauricio;

AUTHOR(S): Nardin, Elizabeth H.; Calvo-Calle, J. Maurici

Oliveira, Giane A.; Nussenzweig, Ruth S.; Schneider, Martin; Tiercy, Jean-Marie; Loutan,

Louis; Hochstrasser, Denis; Rose, Keith

CORPORATE SOURCE: Department of Medical and Molecular

Parasitology, New York University School of

Medicine, New York, NY, 10010, USA

SOURCE: Journal of Immunology (2001), 166(1), 481-489

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal LANGUAGE: English

This open-labeled phase I study provides the first demonstration of the immunogenicity of a precisely defined synthetic polyoxime malaria vaccine in volunteers of diverse HLA types. polyoxime, designated (T1BT\*)4-P3C, was constructed by chemoselective ligation, via oxime bonds, of a tetrabranched core with a peptide module contq. B cell epitopes and a universal T cell epitope of the Plasmodium falciparum circumsporozoite protein. The triepitope polyoxime malaria vaccine was immunogenic in the absence of any exogenous adjuvant, using instead a core modified with the lipopeptide P3C as an endogenous adjuvant. This totally synthetic vaccine formulation can be characterized by mass spectroscopy, thus enabling the reproducible prodn. of precisely defined vaccines for human use. The majority of the polyoxime-immunized volunteers (7/10) developed high levels of anti-repeat Abs that reacted with the native circumsporozoite on P. falciparum sporozoites. In addn., these seven volunteers all developed T cells specific for the universal epitope, termed T\*, which was originally defined using CD4+ T cells from protected volunteers immunized with irradiated P. falciparum sporozoites. excellent correlation of T\*-specific cellular responses with high anti-repeat Ab titers suggests that the T\* epitope functioned as a universal Th cell epitope, as predicted by previous peptide/HLA binding assays and by immunogenicity studies in mice of diverse H-2 haplotypes. The current phase I trial suggests that polyoximes may prove useful for the development of highly immunogenic, multi-component synthetic vaccines for malaria, as well as for other pathogens.

#### IT 329019-45-6P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(a synthetic polyoxime malaria vaccine contg. P. falciparum B cell and universal T cell epitopes eliciting immune responses in diverse HLA haplotypes)

#### TT 151113-09-6P

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(universal T epitope; a synthetic polyoxime malaria vaccine contq. P. falciparum B cell and universal T cell epitopes eliciting immune responses in diverse HLA haplotypes) REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE

FOR THIS RECORD. ALL CITATIONS AVAILABLE

IN THE RE FORMAT

ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2002 ACS 1998:509115 HCAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER: 129:148063

TITLE: Universal T-cell epitopes for anti-

malarial vaccines

INVENTOR(S): Nardin, Elizabeth; Moreno, Alberto

PATENT ASSIGNEE(S): New York University, USA

> 308-4994 Searcher : Shears

PCT Int. Appl., 39 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: KIND DATE APPLICATION NO. DATE PATENT NO. -----\_\_\_\_\_ 19980121 A1 19980723 WO 1998-US1527 WO 9831382 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 1998-59316 19980121 A1 19980807 AU 9859316 20000314 BR 1998-6971 19980121 BR 9806971 Α EP 1998-902726 19980121 EP 1007081 20000614 A1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 1998-534771 19980121 Т2 20010724 JP 2001509813 PRIORITY APPLN. INFO.: US 1997-33916P P 19970121 WO 1998-US1527 W 19980121 The present invention provides methods and compns. for eliciting AB protective immunity against malaria. In particular, the invention relates to universal T-cell epitopes that elicit T-cell responses in individuals of differing genetic backgrounds. Immunogenic compns. and vaccines comprising malaria -specific universal T-cell epitopes are disclosed. 151113-09-6 IT RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (universal T-cell epitopes for anti-malarial vaccines) THERE ARE 5 CITED REFERENCES AVAILABLE FOR 5 REFERENCE COUNT: THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1998:414678 HCAPLUS 129:64049 DOCUMENT NUMBER: Targeted nucleic acid delivery into liver cells TITLE: using circumsporozoite protein complexed with polylysine as nucleic acid carrier Kuo, M. Tien; Ding, Zhi Ming INVENTOR(S): Board of Regents , University of Texas System, PATENT ASSIGNEE(S): USA U.S., 34 pp. SOURCE: CODEN: USXXAM DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT:

Searcher: Shears 308-4994

APPLICATION NO.

DATE

PATENT INFORMATION:

PATENT NO.

KIND

DATE

19980616 US 1995-395602 19950227 Α US 5766899 Disclosed is a receptor-mediated complex that selectively delivers AB nucleic acid into hepatocytes. Circumsporozoite (CS) protein is the targeting ligand that recognizes a receptor expressed on the liver cell surface. The CS ligand is complexed with a polylysine component that can bind nucleic acid. The level of gene expression is greatly enhanced when the complex is cotransfected with adenovirus. Using the present invention, a reporter gene was successfully transferred into a no. of different cell lines that express high levels of receptor. The ability to introduce nucleic acid into specific mammalian cells is an important therapy for numerous diseases such as cancer, malaria and hepatitis.

IT 208947-67-5

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CS antigen fragment; targeted nucleic acid delivery into liver cells using circumsporozoite protein complexed with polylysine as nucleic acid carrier)

REFERENCE COUNT:

29

THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1998:246174 HCAPLUS

DOCUMENT NUMBER:

129:66591

TITLE:

Plasmodium falciparum polyoximes: highly immunogenic synthetic vaccines constructed by chemoselective ligation of repeat B-cell epitopes and a universal T-cell epitope of CS protein

AUTHOR(S):

Nardin, E. H.; Calvo-Calle, J. M.; Oliveira, G. A.; Clavijo, P.; Nussenzweig, R.; Simon, R.;

Zeng, W.; Rose, K.

CORPORATE SOURCE:

Department of Medical and Molecular

Parasitology, New York University School of

Medicine, New York, NY, 10010, USA

SOURCE:

Vaccine (1998), 16(6), 590-600 CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE:

Journal LANGUAGE: English

Effective immunoprophylaxis directed against the pre-erythrocytic stages of the malaria parasite requires a vaccine that can elicit humoral and cell mediated immunity in individuals of diverse genetic background. In order for a synthetic peptide malaria vaccine to meet these requirements, problems assocd. with genetic restriction, peptide chem., adjuvant formulation and physiochem. characterization of the final synthetic vaccine product must first be overcome. To address these issues, five polyoxime vaccine candidates have been constructed by ligating purified peptide epitopes of the P. falciparum CS protein to a branched template via oxime bonds. All five constructs, including two based on templates contg. the synthetic adjuvant tripalmitoyl-S-glyceryl cysteine (Pam3Cys), were of sufficient purity for characterization by mass spectrometry. The immunogenicity of the malaria polyoximes in different murine strains was compared to that of multiple antigen peptide (MAP) constructs synthesized by std.

step-wise synthesis. A tri-epitope polyoxime-Pam3Cys construct, based on the repeats and a universal T-cell epitope that contains both helper and CTL epitopes of the CS protein, was shown to be a precisely-defined synthetic malaria vaccine candidate that was highly immunogenic in murine strains of diverse H-2 haplotypes. 208946-19-4P 208946-20-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(Plasmodium falciparum synthetic vaccines using B-cell and T-cell epitope polyoximes and the antibody response)

IT 151113-09-6P

IT

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(Plasmodium falciparum synthetic vaccines using B-cell and T-cell epitope polyoximes and the antibody response)

L3 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:476523 HCAPLUS

DOCUMENT NUMBER: 127:204127

TITLE: Binding of malaria T cell epitopes to

DR and DQ molecules in vitro correlates with immunogenicity in vivo. Identification of a universal T cell epitope in the Plasmodium

falciparum circumsporozoite protein

AUTHOR(S): Calvo-Calle, J. Mauricio; Hammer, Juergen;

Sinigaglia, Francesco; Clavijo, Pedro; Moya-Castro, Z. Rosa; Nardin, Elizabeth H.

CORPORATE SOURCE: Dep. Medical and Molecular Parasitology, School

Medicine, New York Univ., New York, NY, 10016,

USA

SOURCE: Journal of Immunology (1997), 159(3), 1362-1373

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal LANGUAGE: English

The efficacy of a malaria peptide vaccine would be enhanced by the inclusion of a parasite-derived universal T cell epitope to ensure that all vaccines develop parasite-specific cellular and humoral immunity. Two circumsporozoite (CS) protein T cell epitopes, previously identified by CD4+ T cell clones derived from Plasmodium falciparum sporozoite-immunized volunteers, were studied to det. their HLA class II binding potential. One epitope, located in amino acid (aa) 326-345 of the P. falciparum (NF54 strain) CS protein, was "universal" in that it could bind to multiple DR and DQ mols. in vitro. In contrast, the second epitope, T1, which is located in the CS repeat region, was recognized by T cells in the context of DQ6 (DQB1\*0603) and did not bind with high affinity to any of the class II mols. tested in the peptide binding assays. The in vitro patterns of peptide/HLA interactions correlated with immunogenicity in vivo. A multiple antigen peptide (MAP) contq. the aa 326-345 epitope elicited responses in eight inbred strains (H-2a,b,d,k,p,q,r,s), while the T1 MAP was recognized by only a single haplotype, H-2b. The combination of the universal aa 326-345 T cell epitope and the T1 repeat in a di-epitope MAP overcame the genetic restriction to the P. falciparum CS repeat region and elicited antisporozoite Ab responses in all of the MAP-immunized mice. Synthetic peptide malaria vaccines

contg. the aa 326-345 universal T cell epitope would be expected to elicit parasite-specific immune responses in both sporozoite-primed and naive individuals of diverse genetic backgrounds.

IT 151113-09-6P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(binding of malaria T cell epitopes to human DR and DQ mols. and identification of a universal T cell epitope in the Plasmodium falciparum circumsporozoite protein)

L3 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:647465 HCAPLUS

DOCUMENT NUMBER: 119:247465

TITLE: CD4+ T cell clones obtained from Plasmodium

falciparum sporozoite-immunized volunteers recognize polymorphic sequences of the

circumsporozoite protein

AUTHOR(S): Moreno, Alberto; Clavijo, Pedro; Edelman,

Robert; Davis, Jonathan; Sztein, Marcelo; Sinigaglia, Francesco; Nardin, Elizabeth

CORPORATE SOURCE: Sch. Med., New York Univ., New York, NY, 10010,

USA

SOURCE: Journal of Immunology (1993), 151(1), 489-99

CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal LANGUAGE: English

AB CD4+ T cell clones were derived from three volunteers who were protected against malaria after immunization with Plasmodium falciparum sporozoites. T cells specific for an epitope, Pf Th/Tc, contained in amino acids 326 to 345 of the circumsporozoite (CS) protein of P. falciparum (NF54) were derived from all three volunteers. DR1-, -4-, -7-, and -9-restricted T cell clones were found to recognize overlapping, but distinct, epitopes within a 20-mer peptide representing the amino acid 326 to 345 sequence. The Pf Th/Tc epitope contains part of the highly conserved region II as well as part of a polymorphic domain of the P. falciparum CS protein. All of the overlapping epitopes within peptide 326-345 contained at least three amino acids of the amino terminus of the conserved region II, in addn. to a variable no. of

amino acids in the polymorphic region. The DR4-, -7-, and -9-restricted but not the DR1-restricted T cell clones recognized variant peptides representing this polymorphic region of the CS protein of P. falciparum isolates from Africa, Asia, and South America.

IT **151113-09-6** 

RL: BIOL (Biological study)

(HLA-DR-restricted T cell clone recognition of, of circumsporozoite protein of Plasmodium falciparum in humans)

L3 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:493517 HCAPLUS

DOCUMENT NUMBER: 119:93517

TITLE: Hybrid protein with Plasmodium CS protein sequence and hepatitis B surface antigen

sequence and hepatitis B surface antige sequence, and use for vaccine against

malaria

INVENTOR(S): De Wilde, Michel; Cohen, Joseph

PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	NO.		KI	ND	DATE			P	PPL	ICATI	ON N	0.	DATE		
WO	9310 W:					1993 US			W	10 1	992-E	P259	1	1992	1111	
								FR.	GB,	GR	, IE,	IT,	LU	, MC,	NL,	SE
AU	9229															
EP	6144	65		Α	1	1994	0914		E	P 1	992-9	2348	6	1992	1111	
	6144															
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IE,	IT,	LI	, LU,	MC,	NL,
		SE														
JP	0750	1213		T.	2						992-5					
	1777					1999	0415		P	T 1	992-9	2348	6	1992	1111	
ES	2129	461		T	3	1999	0616		E	S 1	992-9	2348	6			
ZA	9208	770		Α		1994	0513		Z	A 1	992-8	770		1992	1113	
US	5928	902		Α		1999	0727		. U	IS 1	996-7	6079	7	1996	1204	
AU	9714	717		Α	1	1997	0612		P	U 1	997-1	4717		1997	0214	
AU	7124	09		В	2	1999	1104									
US	6169	171		В	1	2001	0102		Ü	s 1	997-9	3292	9	1997	0918	
PRIORIT	Y APP	LN.	INFO	. :				(	GB 1	991	-2439	0	Α	1991	1116	
								1	US 1	992	-8426	94	Α	1992	0227	
								1	wo 1	992	-EP25	91	Α	1992	1111	
								1	US 1	995	-4426	12	В1	1995	0517	
								Į	US 1	996	-6633	71	В1	1996	0613	

Hybrid proteins (RTS and RTS\*) are disclosed which include a portion AΒ of the CS protein of P. falciparum and of the surface antigen of hepatitis B virus (HBsAg). The RTS hybrid consists of (1) a Met residue derived from the Saccharomyces cerevisiae TDH3 gene sequence; (2) a Met-Ala-Pro sequence; (3) a P. falciparum CS protein fragment; (4) an Arg residue; (5) a carboxyl-terminal tetrapeptide sequence (Pro-Val-Thr-Asn) of hepatitis B pre-S2 protein; and (6) hepatitis B S-protein sequence. Also disclosed is a mixed multimeric lipoprotein particle contg. the hybrid protein and HBsAg. The hybrid proteins and particles are useful for antimalaria vaccines. Expression cassette construction is described, and amino acid sequences (and corresponding nucleotide sequences) are included. (RTS,S) lipoprotein particles induced, both in mice and monkeys, a high antibody response directed against the repeat and nonrepeat CS epitopes and against the S protein of the HBsAg carrier. The antibodies elicited in the 2 animal species effectively prevented invasion of cultured human hepatoma cells by P. falciparum sporozoites.

#### IT 149121-48-2

RL: PRP (Properties)

(amino acid sequence of, for vaccine against malaria)

L3 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1992:649667 HCAPLUS

DOCUMENT NUMBER: 117:249667

TITLE: In vitro immune recognition of synthetic

peptides from the Plasmodium falciparum CS protein by individuals naturally exposed to

different sporozoite challenge

AUTHOR(S): Esposito, Fulvio; Lombardi, Stefania; Modiano,

David; Habluetzel, Annette; DelNero, Luca; Lamizana, Lansina; Pietra, Virginio; Rotigliano,

Gianfranco; Corradin, Giampietro; et al.

CORPORATE SOURCE: Dip. Biol. Mol. Cell. Anim., Univ. Camerino,

Camerino, 62032, Italy

SOURCE: Immunology Letters (1992), 33(2), 187-99

CODEN: IMLED6; ISSN: 0165-2478

DOCUMENT TYPE: Journal LANGUAGE: English

The impact of duration and intensity of sporozoite challenge on the AB in vitro cell immune response to synthetic peptides of the circumsporozoite (CS) protein of P. falciparum was investigated in residents of a malaria endemic area in Burkina Faso (West Africa). Lymphocyte proliferation and interferon-.gamma. (IFN-.gamma.) prodn. were used to assess immune recognition of synthetic peptides corresponding to the polymorphic Th2R and Th3R regions, to the conserved CS.T3 sequence, and to NANP and degenerate NVDP repeats. Immune responses were measured in adults and children from a village where they received >100 sporozoite inoculations/yr and in adults living in a town, exposed to a 10-100 times lower challenge. A lifetime intense exposure apparently increased the ability to proliferate in response to most peptides in the rural adults, who all produced antibodies to NANP repeats. Surprisingly, cell cultures from these subjects seldom contained appreciable levels of IFN-.gamma.. In the urban adults, possibly due to the moderate challenge they are exposed to, differences in the proliferative potentials of the peptides were detected. The highest stimulation indexes were obtained with the genetically unrestricted CS.T3 peptide. Remarkably, proliferative responses to Th2R and Th3R correlated with the humoral response to the CS protein, indicating a T helper significance of the epitopes. The differing proliferative potential of the polymorphic epitopes in the urban adults suggests that polymorphism might delay the development of immune responsiveness under conditions of sporadic transmission. children from the highly malarious village displayed the lowest proliferative scores, accompanied by a high prevalence of antibodies to NANP repeats. The hypothesis is thus proposed that a pure B cell reactivity to NANP repeats could ontogenetically precede the mounting of a conventional T-B cooperative immune response.

IT 116111-16-1

RL: BIOL (Biological study)

(CS protein of Plasmodium falciparum immune recognition in humans in sporozoite challenge in relation to)

L3 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:233694 HCAPLUS

DOCUMENT NUMBER: 116:233694

TITLE: Phagocytosis of liposomes by macrophages:

intracellular fate of liposomal malaria

antigen

AUTHOR(S): Verma, Jitendra N.; Wassef, Nabila M.; Wirtz,

Robert A.; Atkinson, Carter T.; Aikawa,

Masamichi; Loomis, Lawrence D.; Alving, Carl R.

CORPORATE SOURCE: Dep. Membr. Biochem., Walter Reed Army Inst.

Res., Washington, DC, 20307-5100, USA

SOURCE: Biochimica et Biophysica Acta (1991), 1066(2),

229-38

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal LANGUAGE: English

Liposomes contg. a synthetic recombinant protein were phagocytosed AB by macrophages, and the internalized protein was recycled to the cell surfaces where it was detected by ELISA. The transit time of the liposome-encapsulated protein from initial phagocytosis of liposomes to appearance of protein on the surfaces of macrophages was detd. by pulse-chase expts. The macrophages were pulsed with liposomes contg. protein and chased with empty liposomes, and vice The amt. and rate of protein antigen expression at the cell versa. surfaces depended on the quantity of encapsulated protein ingested by the macrophages. Although liposomes were rapidly taken up by macrophages, the liposome-encapsulated protein was antigenically expressed for a prolonged period (at least 24 h) on the cell surface. Liposomes were visualized inside vacuoles in the macrophages by immunogold electron microscopy. The liposomes accumulated along the peripheries of the vacuoles and many of them apparently remained intact for a long time (>6 h). However, nonliposomal free protein was also detected in the cytoplasm surrounding these vacuoles, and it was concluded that the free protein in the cytoplasm was probably en route to the macrophage surface. Exposure of the cells to ammonium chloride did not inhibit the appearance of liposomal antigenic epitopes on the cell surface, and this suggests that expression of the liposomal antigenic epitopes at the surface was not a pH-sensitive phenomenon. There was no effect on a liposomal adjuvant, lipid A, on the rate or extent of surface expression of the liposomal protein.

IT 140877-00-5, Antigen R 32NS181 (influenza virus-Plasmodium falciparum 212-amino acid synthetic)

RL: BIOL (Biological study)

(antigen R32NS1, liposomes contg., phagocytosis of, by macrophage, intracellular antigen expression after)

L3 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:490072 HCAPLUS

DOCUMENT NUMBER: 115:90072

TITLE: Toward the elucidation of the mechanism of

attachment and entry of malaria

sporozoites into cells: synthetic polypeptides from the circumsporozoite protein of Plasmodium falciparum bind calcium and interact with model

phospholipid membranes

AUTHOR(S): Verdini, Antonio S.; Chiappinelli, Lorella;

Zanobi, Antonio

CORPORATE SOURCE: Italfarmaco Res. Cent., Cinisello Balsamo,

20092, Italy

SOURCE: Biopolymers (1991), 31(6), 587-94

CODEN: BIPMAA; ISSN: 0006-3525

DOCUMENT TYPE: Journal LANGUAGE: English

LANGUAGE: English

AB The combined use of CD, Fourier transform IR (FTIR), and attenuated total reflectance FTIR spectroscopies revealed that synthetic

polypeptide models of the P. falciparum circumsporozoite (CS) protein repeat domain bind calcium ions in helicogenic environments.

Ca2+-(NANP)n complexes (n .gtoreq. 20) interact vectorially with model phospholipid membranes, orienting their polypeptide axes preferentially along those of the lipid acyl chains. It is proposed that the P. falciparum CS protein central region, rather than acting as a mol. lure helping the parasite to evade host immune control, plays, as a specific Ca2+ macroligand, a crit. functional role during attachment, invasion, and development of the malaria parasite in the hepatic cell.

116111-16-1 TT

RL: BIOL (Biological study)

(calcium binding and phospholipid membrane interactions of, structure and function of circumsporozoite protein of Plasmodium falciparum in relation to)

ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1990:152771 HCAPLUS

DOCUMENT NUMBER:

112:152771

TITLE:

The circumsporozoite protein gene from NF54, a

Plasmodium falciparum isolate used in

malaria vaccine trials

AUTHOR(S):

Caspers, Patrick; Gentz, Reiner; Matile, Hugues;

Pink, J. Richard; Sinigaglia, Francesco

CORPORATE SOURCE:

Cent. Res. Units, F. Hoffmann-La Roche and Co.,

Ltd., Basel, CH-4002, Switz.

SOURCE:

Molecular and Biochemical Parasitology (1989),

35(2), 185-9

CODEN: MBIPDP; ISSN: 0166-6851

DOCUMENT TYPE:

Journal

LANGUAGE:

English

The circumsporozoite protein gene of P. falciparum isolate NF54 was sequenced. The gene encoded a protein of 405 amino acids.

central region of the protein contained 40 repeats of the

Asn-Ala-Asn-Pro sequence. The cloned gene for the circumsporozoite

protein may be used in vaccine prepn.

125854-16-2, Antigen CS (Plasmodium falciparum strain NF54 ΙT

reduced)

RL: PRP (Properties)

(amino acid sequence of)

ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1989:484065 HCAPLUS

DOCUMENT NUMBER:

111:84065

TITLE:

Conjugate malaria vaccine

INVENTOR(S):

Sadoff, Jerald C.; Cryz, Stanley J., Jr.

PATENT ASSIGNEE(S):

Swiss Serum and Vaccine Institute Berne, Switz.

SOURCE:

Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 289110	A2	19881102	EP 1988-300813	19880201
EP 289110	A3	19900124		
R: AT, BE,	CH, DE	, ES, FR, GB,	GR, IT, LI, LU, NL	, SE
CA 1329124				

Shears 308-4994 Searcher :

AU 1988-11188 19880202 19880804 AU 8811188 Α1 19920611 AU 624324 B2 A2 19900125 JP 1988-22669 19880202 JP 02022300 US-1987-9441 19870202 PRIORITY APPLN. INFO .: US 1988-150359 19880129 MARPAT 111:84065 OTHER SOURCE(S): Immunogenic conjugates are prepd. by covalently linking a carrier protein to a peptide forming an antigenic determinant of circumsporozoite protein via at least one spacer mol. The conjugates are vaccines against malaria. Gram neg. outer membrane proteins are treated with an anhydride to form a water-sol. nontoxic carrier protein for use in a conjugate vaccine.

Choleragenoid was coupled to H-(Asn-Pro-Asn-Ala)3-OH using both succinic anhydride and adipic acid dihydrazide to give an

antimalaria conjugate. A response on an ELISA test was seen for 2/3 human volunteers injected i.m. Reactions following vaccination were mild and transient, and std. physiol. tests showed no change

following vaccination, indicating a lack of toxicity. 117924-88-6DP, protein conjugates 122156-87-0DP,

protein conjugates
RL: PREP (Preparation)

(prepn. of, for antimalaria vaccine)

L3 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:34817 HCAPLUS

DOCUMENT NUMBER:

110:34817

TITLE:

Expression in yeast of DNA encoding hepatitis B

surface antigen-heterologous antigen fusion

proteins for use as vaccines

INVENTOR(S):

Cabezon, Teresa; De Wilde, Michel; Harford,

Nigel

PATENT ASSIGNEE(S):

Smith Kline-Rit S. A., Belg.

SOURCE: Eur. Pat. Appl., 101 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 278940 EP 278940	A2 A3	19880817 19881207	EP 1988-870008	19880125
			GR, IT, LI, LU, NL	, SE
ZA 8800488	A	19881026	ZA 1988-488	19880125
SU 1746887	A3	19920707	SU 1988-4355055	19880126
DK 8800431	Α	19880731	DK 1988-431	19880128
AU 8810930	A1	19880804	AU 1988-10930	19880128
NO 8800395	A	19880801	NO 1988-395	19880129
FI 8800428	Α	19880913	FI 1988-428	19880129
JP 01063382	A2	19890309	JP 1988-21137	19880129
DD 274052	A5	19891206	DD 1988-312554	19880129
HU 50876	A2	19900328	HU 1988-409	19880129
DD 284899	A5	19901128	DD 1988-334294	19880129
DD 285612	A5	19901219	DD 1988-334296	19880129
DD 285994	A5	19910110	DD 1988-334295	19880129
CN 1031395	Α	19890301	CN 1988-100483	19880130
PRIORITY APPLN. INFO.:			US 1987-9325	19870130

Plasmids contg. DNA encoding part or all of the pre-S region of AB hepatitis B surface antigen (HBsAg) fused to DNA encoding an heterologous antigen (e.g. a Plasmodium circumsporozoite (CS) protein epitope, an HIV antigenic peptide) are constructed and expressed in yeast. Immunogenic particles are produced which can be used as vaccines. Plasmid pRIT12574, encoding a fusion protein of pre-S2 HBsAg and tetrapeptide repeats of the Plasmodium CS protein, was constructed. Yeast transformed with this plasmid produced 22 nm-like particles which were purified in the customary manner from the cell ext. Rabbits immunized with these particles developed antibodies to both CS and HBsAg. Sera from these rabbits reacted strongly in a CS pptn. reaction and inhibited sporozoite invasion on hepatoma cells in vitro.

92480-13-2, Antigen CS (Plasmodium falciparum clone 7G8 IT

surface precursor reduced)

RL: PRP (Properties)

(amino acid sequence of)

ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2002 ACS L3

1989:5809 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 110:5809

Reversed-phase liquid chromatography and sodium TITLE:

dodecyl sulfate polyacrylamide gel

electrophoresis characteristics of a recombinant

DNA derived malaria antigen

Benedek, K.; Hughes, B.; Seaman, M. B.; Swadesh, AUTHOR(S):

J. K.

Smith Kline and French Lab., King of Prussia, CORPORATE SOURCE:

PA, 19406-0939, USA

Journal of Chromatography (1988), 444, 191-202 SOURCE:

CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

English LANGUAGE:

Results are presented from anal. of a sample of SK&F 105154 AB (R32NS181), a amalaria vaccine candidate produced in Escherichia coli, and some anal. issues of general relevance to the characterization of such products derived from recombinant DNA technol. are discussed. Anomalous migration and staining behavior were obsd. in SDS-PAGE. Reversed-phase liq. chromatog. (RPLC) appeared to resolve 4 minor components from the principal band, but the minor peaks were found to consist of numerous components resolvable by SDS-PAGE. Western blotting visualized certain components that were not adequately stained by either Coomassie or Ag stain. None of the techniques that were employed were individually adequate to characterize the sample, but, taken together, were adequate to characterize the sample and to identify one principal degrdn. pathway. Degrdn. within the NS181 region decreases the RPLC retention time, while degrdn. within the R32 segment increases the retention time.

117924-89-7 TΨ

RL: BIOL (Biological study)

(as malaria vaccine candidate, characterization of, methods for)

ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2002 ACS L3

1988:529704 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 109:129704

Preparation of immunologically active peptides TITLE:

> Shears 308-4994 Searcher :

for preparation of malaria vaccines

and for detection of antibodies

INVENTOR(S): Bernardi, Adriano; Bonelli, Fabio; Pessi,

Antonello; Verdini, Antonio Silvio

PATENT ASSIGNEE(S): Eniricerche S.p.A., Italy

SOURCE: Ger. Offen., 7 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3741183	A1	19880609	DE 1987-3741183	19871204
DE 3741183	C2	19910606		
ZA 8708903	Α	19880727	ZA 1987-8903	19871126
CH 672491	Α	19891130	CH 1987-4640	19871127
SE 8704765	Α	19880605	SE 1987-4765	19871130
GB 2199038	A1	19880629	GB 1987-28000	19871130
GB 2199038	B2	19910320		
BE 1001692	A5	19900213	BE 1987-1373	19871202
FR 2607703	A1	19880610	FR 1987-16809	19871203
FR 2607703	B1	19930924		
NL 8702921	Α	19880701	NL 1987-2921	19871203
US 4843146	Α	19890627	US 1987-128082	19871203
CA 1304888	A1	19920707	CA 1987-553481	19871203
AT 8703190	Α	19940415	AT 1987-3190	19871203
ES 2005753	A6	19890316	ES 1987-3801	19871204
PRIORITY APPLN. IN	FO.:		IT 1986-22560	19861204

AB H-(Asn-Val-Asp-Pro-Asn-Ala-Asn-Pro)3-(Asn-Ala-Asn-Pro)n-Asn-Ala-OH (I; n .gtoreq. 3) were prepd. for prepn. of malaria vaccines and for use in diagnostic kits for detecting antisporozoite antibodies. I (n = 3) (II) was prepd. on pepsyn A resin contg. p-hydroxymethylphenoxyacetate "hooks" using FMOC-protected amino acid anhydrides.

#### IT 116111-16-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, for prepn. of malaria vaccine and for detection of malaria antibodies)

IT 116111-20-7D, hydroxymethylphenoxyacetate resin-bound

RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, in prepn. of malaria intermediate)

L3 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1985:198973 HCAPLUS

DOCUMENT NUMBER:

102:198973

TITLE:

Immunologically active peptides capable of

inducing immunization against malaria

and genes encoding for them

PATENT ASSIGNEE(S):

United States Dept. of the Army, USA

SOURCE:

U. S. Pat. Appl., 55 pp. Avail. NTIS Order No.

PAT-APPL-6-624 564

CODEN: XAXXAV

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.		KIND	DATE		AF	PLICATION NO.	DATE
	624564		A0	19850104		US	3 1984-624564	19840626
US	4707357		Α	19871117				
ZA	8504697		Α	19860226		$z_{P}$	1985-4697	19850621
EΡ	166410		A2	19860102		ΕP	1985-107794	19850624
ΕP	166410		A3	19871125				
EΡ	166410		B1	19921125				
	R: BE,	CH,	DE, FR	, GB, IT,	LI,	NL,	SE	
ΑU	8543990		A1	19860102			J 1985-43990	19850624
ΑU	596561		B2	19900510				
CA	1340431		A1	19990316		CA	1985-485166	19850625
DK	8502891		Α	19851227		DK	1985-2891	19850626
DK	166284		В	19930329				
DK	166284		С	19930823				
JP	61149093		A2	19860707		JF	1985-140108	19850626
JP	2561238		B2	19961204				
DK	9101919		Α	19911126		DK	( 1991-1919	19911126
DK	166155		В	19930315				
DK	166155		С	19930809				
JP	06225768		A2	19940816		JF	1993-268294	19930930
JP	07110876	;	B4	19951129				
JР	07265086	;	A2	19951017		JF	1995-40679	19950228
JΡ	2537027		B2	19960925				
JР	07265087		A2	19951017		JF	1995-40692	19950228
JP	2537028		B2	19960925				
	APPLN.	INFO.	:		1	US 19	84-624564	19840626

Circumsporozoite proteins or fractions thereof capable of eliciting an immunol. response in humans against Plasmodium falciparum ( malaria) sporozoites are synthesized by peptide coupling reactions on a solid support or by mol. cloning. In the latter case, DNA sequences encoding these immunol. active peptides are cloned on phage .lambda.mPfl and used to lysogenize Escherichia coli from which the peptides are harvested. Thus, cloned DNA sequences from a P. falciparum gene library were obtained that encode a peptide including the major monoclonal antibody binding sequences (1) 2 consecutive Asn-X-Y-Pro repeats, where x is alanine or valine and Y is asparagine or aspartic acid, (2) Thr-Glu-Trp-Z-Pro-Cys-Ser-Val-Thr-Cys-Gly-Asn-Gly, where Z is serine or threonine, or (3) Lys-Pro-S-T-S-Lys-Leu-Lys-Gln-Pro-U-V-Gly-W-Pro, where S is lysine or asparagine, T is histidine or glutamic acid, U is glycine or asparagine, V is aspartic acid or glutamic acid, and W is asparagine or glutamine. The immunol. active peptides formed by E. coli transformed with these DNA sequences when purified and administered i.m. to i.v. at 0.01-100 .mu.g/kg body wt. provide protection against P. faliciparum sporozoite infection.

IT 92480-13-2 92480-14-3

RL: PRP (Properties)

(amino acid sequence of)

IT 96281-87-7P

RL: PREP (Preparation)

(prepn. of, for antimalarial vaccine prodn.)

L3 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:564640 HCAPLUS

DOCUMENT NUMBER: 101:164640

TITLE: Structure of the gene encoding the

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immunodominant surface antigen on the sporozoite
                         of the human malaria parasite
                         Plasmodium falciparum
                         Dame, John B.; Williams, Jackie L.; McCutchan,
AUTHOR(S):
                         Thomas F.; Weber, James L.; Wirtz, Robert A.;
                         Hockmeyer, Wayne T.; Maloy, W. Lee; Haynes, J.
                         David; Schneider, Imogene; et al.
                         Lab. Parasit. Dis., Natl. Inst. Allergy Infect.
CORPORATE SOURCE:
                         Dis., Bethesda, MD, 20205, USA
                         Science (Washington, DC, United States) (1984),
SOURCE:
                         225(4662), 593-9
                         CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
     The gene for the circumsporozoite (CS) protein of P. falciparum was
AB
     cloned, and its nucleotide sequence was detd. The gene encodes a
     protein of 412 amino acids, as deduced from the nucleotide sequence.
     The protein contains 41 tandem repeats of a tetrapeptide, 37 of
     which are Asn-Ala-Asn-Pro [92463-34-8] and 4 of which are
     Asn-Val-Asp-Pro [92463-35-9]. Monoclonal antibodies against the CS
     protein of P. falciparum were inhibited from binding to the protein
     by synthetic peptides of the repeat sequence. The CS protein of P.
     falciparum and the CS protein of a simian malaria
     parasite, P. knowlesi, have 2 regions of homol., 1 of which is
     present on either side of the repeat. One region contains 12 of 13
     identical amino acids. Within the nucleotide sequence of this
     region, 25 of 27 nucleotides are conserved. The conservation of
     these regions in parasites widely sepd. in evolution suggests that
     they may have a function, such as binding to liver cells, and may
     represent an invariant target for immunity.
TΤ
     92480-13-2 92480-14-3
     RL: PRP (Properties)
        (amino acid sequence of)
E1 THROUGH E29 ASSIGNED
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                140877-00-5/BI OR 149121-48-2/BI OR 208946-19-4/BI OR
                208946-20-7/BI OR 208947-67-5/BI OR 329019-45-6/BI OR
                401460-45-5/BI OR 401552-42-9/BI OR 401556-50-1/BI OR
                401556-53-4/BI OR 407646-80-4/BI OR 467522-97-0/BI OR
                96281-87-7/BI)
\Rightarrow s 14 and 11
            29 L4 AND L1
L5
     ANSWER 1 OF 29 REGISTRY COPYRIGHT 2002 ACS
L.5
     467522-97-0 REGISTRY
RN
     Protein (Plasmodium falciparum strain 3D7 clone MAL3P2 gene
     PFC0210c) (9CI)
                     (CA INDEX NAME)
OTHER NAMES:
CN
     GenBank AL034558-derived protein GI 4493889
```

Searcher :

Shears

308-4994

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CI
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SQL
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       1 MRKLAILSVS SFLFVEALFQ EYQCYGSSSN TRVLNELNYD NAGTNLYNEL
SEO
      51 EMNYYGKQEN WYSLKKNSRS LGENDDGNNE DNEKLRKPKH KKLKQPADGN
     101 PDPNANPNVD PNANPNVDPN ANPNVDPNAN PNANPNANPN ANPNANPNAN
                          251 PNANPNANPN ANPNANPNAN PNKNNQGNGQ GHNMPNDPNR NVDENANANS
      301 AVKNNNNEEP SDKHIKEYLN KIQNSLSTEW SPCSVTCGNG IQVRIKPGSA
                       ----
      351 NKPKDELDYA NDIEKKICKM EKCSSVFNVV NSSIGLIMVL SFLFLN
HITS AT:
         120-139, 192-211, 317-336
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
REFERENCE
          1: 137:289735
    ANSWER 2 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    407646-80-4 REGISTRY
RN
    Circumsporozoite protein (Plasmodium falciparum strain FCC-1/HN gene
CN
    csp fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
    GenBank AF315469-derived protein GI 11527999
CN
CI
SOL
   383
       1 FQEYQCYGSS SNTRVLNELN YDNAGTNLYN ELEMNYYGKQ ENWYSLKKNS
SEQ
      51 RSLGENDDGN NNNGDNGREG KDEDKRDGNN EDNEKLRKPK HKKLKQPGDG
      101 NPDPNANPNV DPNANPNVDP NANPNVDPNA NPNANPNANP NANPNANPNA
                           ______
     151 NPNANPNANP NANPNANPNA NPNANPNANP NVDPNANPNA NPNANPNANP
                                ____ ____________
      301 OGHNMPNDPN RNVDENANAN NAVKNNNNEE PSDKHIEQYL KKIQYSLSTE
      351 WSPCSVTCGN GIQVRIKPGS ADKPKDELDY END
HITS AT:
         121-140, 177-196
         1: 136:289638
REFERENCE
    ANSWER 3 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
RN
    401556-53-4 REGISTRY
    130: PN: WO0214478 SEQID: 267 unclaimed protein (9CI) (CA INDEX
CN
    NAME)
    MAN
CI
SQL
   191
       1 MDIDPYKEFG ATVELLSFLP SDFFPSVRDL LDTASALYRE ALESPEHCSP
SEQ
      51 HHTALRQAIL CWGELMTLAT WVGVNLEDGI NANPNANPNA NPNANPELPA
      101 SRDLVVSYVN TNMGLKFRQL LWFHISCLTF GRETVIEYLV SFGVWIRTPP
      151 AYRPPNAPIL STLPETTVVG IEYLNKIQNS LSTEWSPCSV T
                            -------
HITS AT:
         171-191
```

REFERENCE 1: 136:215388 ANSWER 4 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 RN 401556-50-1 REGISTRY 122: PN: WO0214478 SEQID: 263 unclaimed DNA (9CI) (CA INDEX NAME) CN CI MAN 171 SQL 1 MDIDPYKEFG ATVELLSFLP SDFFPSVRDL LDTASALYRE ALESPEHCSP SEQ 51 HHTALRQAIL CWGELMTLAT WVGVNLEDPA SRDLVVSYVN TNMGLKFRQL 101 LWFHISCLTF GRETVIEYLV SFGVWIRTPP AYRPPNAPIL STLPETTVVG 151 IEYLNKIQNS LSTEWSPCSV T 151-171 HITS AT: 1: 136:215388 REFERENCE ANSWER 5 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 401552-42-9 REGISTRY RN Antigen CS (Plasmodium falciparum clone V12.pf3.1) (9CI) (CA INDEX CN NAME) OTHER NAMES: 270: PN: WO0214478 SEQID: 269 claimed protein CN CI SQL 195 1 MDIDPYKEFG ATVELLSFLP SDFFPSVRDL LDTASALYRE ALESPEHCSP SEQ 51 HHTALROAIL CWGELMTLAT WVGVNLEDGI NANPNVDPNA NPNANPNANP \_\_\_\_\_\_ 101 ELPASRDLVV SYVNTNMGLK FRQLLWFHIS CLTFGRETVI EYLVSFGVWI 151 RTPPAYRPPN APILSTLPET TVVGIEYLNK IQNSLSTEWS PCSVT 81-100, 175-195 HITS AT: 1: 136:215388 REFERENCE ANSWER 6 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 401461-03-8 REGISTRY RN L-Threonine, L-threonyl-L-threonyl-L-valyl-L-valylglycyl-L-isoleucyl-CN L-.alpha.-glutamyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-lysyl-Lisoleucyl-L-qlutaminyl-L-asparaginyl-L-seryl-L-leucyl-L-seryl-Lthreonyl-L-.alpha.-glutamyl-L-tryptophyl-L-seryl-L-prolyl-Lcysteinyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME) OTHER NAMES: 183: PN: WO0213765 SEQID: 166 unclaimed sequence CN 284: PN: WOO214478 SEQID: 283 claimed sequence CN SQL 26 1 TTVVGIEYLN KIQNSLSTEW SPCSVT SEO ---- ------ -----HITS AT: 6-26 1: 136:215388 REFERENCE REFERENCE 136:198912 2: ANSWER 7 OF 29 REGISTRY COPYRIGHT 2002 ACS L5RN 401460-60-4 REGISTRY

```
L-Threonine, L-isoleucyl-L-alpha.-glutamyl-L-tyrosyl-L-leucyl-L-
CN
     asparaginyl-L-lysyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-seryl-L-
     leucyl-L-seryl-L-threonyl-L-.alpha.-glutamyl-L-tryptophyl-L-seryl-L-
     prolyl-L-cysteinyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
     121: PN: WOO214478 SEQID: 120 claimed sequence
     95: PN: WO0213765 SEQID: 79 unclaimed sequence
CN
SQL
         1 IEYLNKIQNS LSTEWSPCSV T
SEQ
           HITS AT:
          1-21
           1: 136:215388
REFERENCE
               136:198912
REFERENCE
           2:
    ANSWER 8 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    401460-49-9 REGISTRY
RN
    L-Leucine, L-isoleucyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-
CN
    L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-
     alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-.alpha.-
     glutamyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
    83: PN: WOO213765 SEQID: 43 unclaimed sequence
     85: PN: WO0214478 SEQID: 84 claimed sequence
CN
SOL
        1 INANPNVDPN ANPNANPNAN PEL
SEQ
           ______
          2-21
HITS AT:
           1: 136:215388
REFERENCE
REFERENCE
           2:
               136:198912
    ANSWER 9 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
     401460-48-8 REGISTRY
RN
    L-Leucine, L-isoleucyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-
CN
     L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-
     alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
     valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-
     asparaginyl-L-prolyl-L-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
    82: PN: WO0213765 SEQID: 40 unclaimed sequence
CN
     82: PN: WOO214478 SEQID: 81 claimed sequence
CN
SQL
SEQ
         1 INANPNVDPN ANPNANPNAN PNVDPNANPE L
           HITS AT:
         2-21
REFERENCE
           1: 136:215388
REFERENCE
           2: 136:198912
```

```
ANSWER 10 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    401460-45-5 REGISTRY
RN
    L-Threonine, glycyl-L-isoleucyl-L-.alpha.-glutamyl-L-tyrosyl-L-
CN
    leucyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-
    L-seryl-L-leucyl-L-seryl-L-threonyl-L-.alpha.-glutamyl-L-tryptophyl-
    L-seryl-L-prolyl-L-cysteinyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
    78: PN: WOO213765 SEQID: 24 claimed sequence
SQL
        1 GIEYLNKIQN SLSTEWSPCS VT
SEQ
           HITS AT:
          2-22
           1: 136:198912
REFERENCE
    ANSWER 11 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    401460-29-5 REGISTRY
RN
    L-Proline, L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-
CN
    asparaginyl-L-valyl-L-alpha.-aspartyl-L-prolyl-L-asparaginyl-L-
    alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
    valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-
    asparaginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
    25: PN: WO0214478 SEQID: 24 claimed sequence
    59: PN: WOO213765 SEQID: 5 claimed sequence
CN
SQL
        1 NANPNVDPNA NPNANPNANP NVDPNANP
SEQ
          _____
          1-20
HITS AT:
               136:215388
REFERENCE
           1:
REFERENCE
           2:
               136:198912
    ANSWER 12 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    401460-27-3 REGISTRY
RN
    L-Proline, L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-
CN
    asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-
    alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
    23: PN: WOO214478 SEQID: 22 claimed sequence
CN
    57: PN: WOO213765 SEQID: 3 claimed sequence
CN
SQL
    20
        1 NANPNVDPNA NPNANPNANP
SEQ
          HITS AT:
          1-20
               137:92286
REFERENCE
           1:
               136:215388
REFERENCE
           2:
REFERENCE
           3:
               136:198912
```

ANSWER 13 OF 29 REGISTRY COPYRIGHT 2002 ACS L5RN **401460-26-2** REGISTRY L-Proline, L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-CN asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-Lalanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-Lprolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-Lvaly1-L-.alpha.-asparty1- (9CI) (CA INDEX NAME) OTHER NAMES: 22: PN: WOO214478 SEQID: 21 claimed sequence CN 56: PN: WO0213765 SEQID: 2 claimed sequence CN SQL 1 NANPNVDPNA NPNANPNANP NVDP SEO 1-20 HITS AT: 136:215388 1: REFERENCE 136:198912 REFERENCE 2: ANSWER 14 OF 29 REGISTRY COPYRIGHT 2002 ACS L5329019-45-6 REGISTRY RN L-Lysine, N2,N6-bis[N2,N6-bis(L-.alpha.-aspartyl-L-prolyl-L-CN asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-Lprolyl-L-asparaginyl-L-valyl-L-asparaginyl-L-alanyl-L-asparaginyl-Lprolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-Lalanyl-L-asparaginyl-L-prolyl-L-.alpha.-glutamyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-lysyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-seryl-L-leucyl-L-seryl-L-threonyl-L-.alpha.-glutamyl-L-tryptophyl-L-seryl-L-prolyl-L-cysteinyl-L-seryl-L-valyl-L-threonyl)-L-lysyl]-L-lysyl-Lseryl-L-seryl-N6-[S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-N-(1oxohexadecyl)-L-cysteinyl]-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-lysyl-(CA INDEX NAME) (9CI) CI MAN 204,58,49,48,48,1 SQL 1 DPNANPNVDP NANPNVNANP NANPNANPEY LNKIQNSLST EWSPCSVTKK SEO \_\_ \_\_\_\_\_ 51 SSKSKKKK HITS AT: 29-48 1 DPNANPNVDP NANPNVNANP NANPNANPEY LNKIQNSLST EWSPCSVTK SEO HITS AT: 29-48 1 DPNANPNVDP NANPNVNANP NANPNANPEY LNKIQNSLST EWSPCSVT SEQ HITS AT: 29-48 1 DPNANPNVDP NANPNVNANP NANPNANPEY LNKIQNSLST EWSPCSVT SEO HITS AT: 29 - 48SEQ 1 C · REFERENCE 1: 134:221126

```
ANSWER 15 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    208947-67-5 REGISTRY
RN
    Circumsporozoite antigen (Plasmodium falciparum fragment) (9CI)
                                                                   (CA
CN
    INDEX NAME)
CI
    MAN
SOL
    126
        1 NANPNVDPNA NPNVDPNANP NVDPNANPNA NPNANPNANP NANPNANPNA
SEQ
                          ____ _______________
       101 NANPNANPEW SPCSVTCGNG IQVRIK
HITS AT:
          17-36
               129:64049
REFERENCE
           1:
    ANSWER 16 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
RN
    208946-20-7 REGISTRY
    L-Threonine, L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-
CN
    asparaginyl-L-prolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
    valyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
    alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-.alpha.-glutamyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-lysyl-L-
    isoleucyl-L-glutaminyl-L-asparaginyl-L-seryl-L-leucyl-L-seryl-L-
    threonyl-L-.alpha.-glutamyl-L-tryptophyl-L-seryl-L-prolyl-L-
    cysteinyl-L-seryl-L-valyl-, 1,1',1'',1'''-tetraamide with
    N2,N6-bis[N2,N6-bis[[(carboxymethyl)oxidoimino]methyl]-L-lysyl]-L-
    lysyl-L-tyrosine (9CI)
                          (CA INDEX NAME)
CI
    MAN
    200, 49, 49, 49, 49, 3, 1
SOL
SEQ
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
                                        HITS AT:
          30 - 49
SEQ
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
                                        _ ______ ___
HITS AT:
          30 - 49
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEO
                                        HITS AT:
          30 - 49
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEQ
                                        _ ______ ____
HITS AT:
          30 - 49
        1 KKY
SEQ
SEO
        1 K
           1: 129:66591
REFERENCE
    ANSWER 17 OF 29 REGISTRY COPYRIGHT 2002 ACS
L_5
RN
    208946-19-4 REGISTRY
    L-Threonine, L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-
CN
    asparaginyl-L-prolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-
    prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
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valyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-
    alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-
    prolyl-L-.alpha.-glutamyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-lysyl-L-
    isoleucyl-L-glutaminyl-L-asparaginyl-L-seryl-L-leucyl-L-seryl-L-
    threonyl-L-.alpha.-glutamyl-L-tryptophyl-L-seryl-L-prolyl-L-
    cysteinyl-L-seryl-L-valyl-, 1,1',1'',1'''-tetraamide with
    N2, N6-bis[N2, N6-bis[[(carboxymethyl)oxidoimino]methyl]-L-lysyl]-L-
    lysyl-L-seryl-L-seryl-N6-[S-[2,3-bis[(1-oxohexadecyl)oxy]propyl]-N-
     (1-oxohexadecyl)-L-cysteinyl]-L-lysyl-L-seryl-L-lysyl-L-lysyl-L-
    lysyl-L-lysine (9CI) (CA INDEX NAME)
CI
    MAN
    208, 49, 49, 49, 49, 10, 1, 1
SOL
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEO
                                        HITS AT:
          30-49
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEQ
                                        HITS AT:
          30-49
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEQ
                                        _ ____
HITS AT:
          30 - 49
        1 GDPNANPNVD PNANPNVNAN PNANPNANPE YLNKIQNSLS TEWSPCSVT
SEO
                                        HITS AT:
          30 - 49
        1 KKSSKSKKKK
SEQ
SEQ
        1 C
        1 K
SEQ
REFERENCE
           1: 129:66591
    ANSWER 18 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
   151113-09-6 REGISTRY
RN
    L-Threonine, L-.alpha.-glutamyl-L-tyrosyl-L-leucyl-L-asparaginyl-L-
CN
    lysyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-L-seryl-L-leucyl-L-
    seryl-L-threonyl-L-alpha.-glutamyl-L-tryptophyl-L-seryl-L-prolyl-L-
    cysteinyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN
    166: PN: WOO213765 SEQID: 148 claimed sequence
     60: PN: WO0214478 SEQID: 59 claimed sequence
CN
SQL 20
SEO
        1 EYLNKIONSL STEWSPCSVT
          HITS AT:
          1-20
REFERENCE
           1:
               136:215388
REFERENCE
           2:
               136:198912
REFERÈNCE
           3: 134:221126
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129:148063 REFERENCE 4: REFERENCE 5: 129:66591 REFERENCE 6: 127:204127 REFERENCE 7: 119:247465 ANSWER 19 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 RN 149121-48-2 REGISTRY 207-404-Antigen CS (Plasmodium falciparum strain NF54 reduced), CN 207-L-methionine-208-L-methionine-209-L-alanine-210-L-proline-400glycine-401-L-proline-403-L-threonine-404-L-asparagine-, (404.fwdarw.1')-protein with antigen (hepatitis B virus subtype adw small surface reduced) (9CI) (CA INDEX NAME) CI MAN SOL 424 SEQ 51 NANPNANPNA NPNANPNANP NANPNANPNK NNQGNGQGHN MPNDPNRNVD 101 ENANANSAVK NNNNEEPSDK HIKEYLNKIQ NSLSTEWSPC SVTCGNGIQV 151 RIKPGSANKP KDELDYANDI EKKICKMEKC SSVFNVVNSS IGLGPVTNME 201 NITSGFLGPL LVLQAGFFLL TRILTIPQSL DSWWTSLNFL GGSPVCLGQN 251 SQSPTSNHSP TSCPPICPGY RWMCLRRFII FLFILLLCLI FLLVLLDYQG 301 MLPVCPLIPG STTTNTGPCK TCTTPAQGNS MFPSCCCTKP TDGNCTCIPI 351 PSSWAFAKYL WEWASVRFSW LSLLVPFVQW FVGLSPTVWL SAIWMMWYWG 401 PSLYSIVSPF IPLLPIFFCL WVYI HITS AT: 124-143 REFERENCE 1: 119:93517 ANSWER 20 OF 29 REGISTRY COPYRIGHT 2002 ACS L5RN 140877-00-5 REGISTRY Antigen R 32NS181 (influenza virus-Plasmodium falciparum 212-amino CN acid synthetic) (9CI) (CA INDEX NAME) CI MAN SQL 212 SEO 51 PNANPNANPN ANPNVDPNAN PNANPNANPN ANPNANPNAN PNANPNANPN 101 ANPNANPNAN PNANPNANPN ANPNANPNVD PNTVSSFQVD CFLWHVRKRV 151 ADQELGDAPF LDRLRRDQKS LRGRGSTLGL DIETATRAGK QIVERILKEE 201 SDEALKMTML VN HITS AT: 60-79 REFERENCE 1: 116:233694 ANSWER 21 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 125854-16-2 REGISTRY RN Antigen CS (Plasmodium falciparum strain NF54 reduced) (9CI) (CA CN INDEX NAME) MAN CT SQL 409 1 MMRKLAILSV SSFLFVEALF QEYQCYGSSS NTRVLNELNY DNAGTNLYNE SEO 51 LEMNYYGKQE NWYSLKKNSR SLGENDDGNN EDNEKLRKPK HKKLKQPADG

```
101 NPDPNANPNV DPNANPNVDP NANPNVDPNA NPNANPNANP NANPNANPNA
                           ______
      251 NPNANPNANP NANPNANPNA NPNANPNANP NANPNKNNQG NGQGHNMPND
      301 PNRNVDENAN ANSAVKNNNN EEPSDKHIKE YLNKIQNSLS TEWSPCSVTC
                                   351 GNGIQVRIKP GSANKPKDEL DYANDIEKKI CKMEKCSSVF NVVNSSIGLI
      401 MVLSFLFLN
         121-140, 205-224, 330-349
HITS AT:
REFERENCE
          1: 112:152771
    ANSWER 22 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    122156-87-0 REGISTRY
RN
    129-259-Antigen CS (Plasmodium falciparum clone 7G8 surface
CN
    reduced), 129-L-methionine-257-L-valine-258-L-aspartic acid- (9CI)
    (CA INDEX NAME)
CI
    MAN
SQL
   131
       SEQ
      51 PNANPNANPN ANPNVDPNAN PNANPNANPN ANPNANPNAN PNANPNANPN
                = ==========
      101 ANPNANPNAN PNANPNANPN ANPNANPNVD P
HITS AT:
         60-79
REFERENCE
          1: 111:84065
    ANSWER 23 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    117924-89-7 REGISTRY
RN
    126-261-Antigen CS (Plasmodium falciparum clone 7G8 surface
CN
    reduced), 129-L-methionine-257-L-valine-258-L-aspartic
    acid-260-L-leucine-261-L-arginine-, (261.fwdarw.4')-protein with
    44-L-arginine-53-L-aspartic acid-60-L-alanine-82-L-leucine-83-L-
    valine-84-L-asparagine-4-84-protein NS 1 (influenza virus A/FM/1/47
    reduced) (9CI) (CA INDEX NAME)
CI
    MAN
SQL 220
       SEO
      51 PNANPNANPN ANPNANPNVD PNANPNANPN ANPNANPNAN PNANPNANPN
                     101 ANPNANPNAN PNANPNANPN ANPNANPNAN PNANPNVDPN TVSSFQVDCF
      151 LWHVRKRVAD QELGDAPFLD RLRRDQKSLR GRGSTLGLDI ETATRAGKQI
      201 VERILKEESD EALKMTMLVN
         64-83
HITS AT:
REFERENCE
          1: 110:5809
    ANSWER 24 OF 29 REGISTRY COPYRIGHT 2002 ACS
L5
    117924-88-6 REGISTRY
RN
    129-261-Antigen CS (Plasmodium falciparum clone 7G8 surface
CN
    reduced), 129-L-methionine-257-L-valine-258-L-aspartic
    acid-260-L-leucine-261-L-arginine- (9CI) (CA INDEX NAME)
CI
    MAN
SQL 125
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SEQ ===== ===== 101 ANPNANPNAN PNANPNANPN VDPLR 56-75 HITS AT: 1: 111:84065 REFERENCE 110:13419 REFERENCE 2: ANSWER 25 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 RN 116111-20-7 REGISTRY L-Alanine, N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-asparaginyl-L-CN valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-Lasparaginyl-L-prolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-Lprolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-Lvalvl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-Lasparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-Lasparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-Lasparaginyl-L-prolyl-L-asparaginyl- (9CI) (CA INDEX NAME) CI MAN SQL 38 SEQ 1 NVDPNANPNV DPNANPNVDP NANPNANPNA NPNANPNA HITS AT: 13-32 \*\*RELATED SEOUENCES AVAILABLE WITH SEQLINK\*\* REFERENCE 1: 109:129704 ANSWER 26 OF 29 REGISTRY COPYRIGHT 2002 ACS L5RN **116111-16-1** REGISTRY CN L-Alanine, L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-Lasparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-Lprolyl-L-asparaginyl-L-valyl-L-.alpha.-aspartyl-L-prolyl-Lasparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl-L-alanyl-Lasparaginyl-L-prolyl-L-asparaginyl-L-alanyl-L-asparaginyl-L-prolyl-Lasparaginyl-L-alanyl-L-asparaginyl-L-prolyl-L-asparaginyl- (9CI) (CA INDEX NAME) CI MAN SQL 38 SEQ 1 NVDPNANPNV DPNANPNVDP NANPNANPNA NPNANPNA \_\_\_\_\_\_ \_\_\_ HITS AT: 13-32 \*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\* REFERENCE 1: 117:249667 REFERENCE 115:90072 2: REFERENCE 109:129704 3: ANSWER 27 OF 29 REGISTRY COPYRIGHT 2002 ACS **L**5

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96281-87-7 REGISTRY RN 91-340-Antigen CS (Plasmodium falciparum clone 7G8 surface reduced) CN (9CI) (CA INDEX NAME) CI MAN SQL 250 1 KPKHKKLKQP GDGNPDPNAN PNVDPNANPN VDPNANPNVD PNANPNANPN SEO \_\_\_\_\_ 151 ANPNANPNAN PNANPNANPN ANPNANPNAN PNKNNQGNGQ GHNMPNDPNR 201 NVDENANANN AVKNNNNEEP SDKHIEQYLK KIKNSISTEW SPCSVTCGNG 34-53, 98-117 HITS AT: REFERENCE 1: 102:198973 ANSWER 28 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 RN **92480-14-3** REGISTRY Antigen CS (Plasmodium falciparum clone 7G8 surface reduced) (9CI) CN (CA INDEX NAME) CI MAN SQL 396 1 EALFQEYQCY GSSSNTRVLN ELNYDNAGTN LYNELEMNYY GKQENWYSLK SEO 51 KNSRSLGEND DGNNNNGDNG REGKDEDKRD GNNEDNEKLR KPKHKKLKQP 101 GDGNPDPNAN PNVDPNANPN VDPNANPNVD PNANPNANPN ANPNANPNAN \_\_\_\_\_ \_\_\_ \_\_\_ \_\_\_\_\_ 251 PNANPNANPN ANPNANPNAN PNKNNQGNGQ GHNMPNDPNR NVDENANANN 301 AVKNNNNEEP SDKHIEQYLK KIKNSISTEW SPCSVTCGNG IQVRIKPGSA 351 NKPKDELDYE NDIEKKICKM EKCSSVFNVV NSSIGLIMVL SFLFLN 124-143, 188-207 HITS AT: REFERENCE 1: 102:198973 REFERENCE 2: 101:164640 ANSWER 29 OF 29 REGISTRY COPYRIGHT 2002 ACS L5 RN **92480-13-2** REGISTRY Antigen CS (Plasmodium falciparum clone 7G8 surface precursor CN reduced) (9CI) (CA INDEX NAME) CI MAN L 412 SEO 1 MMRKLAILSV SSFLFVEALF QEYQCYGSSS NTRVLNELNY DNAGTNLYNE 51 LEMNYYGKOE NWYSLKKNSR SLGENDDGNN NNGDNGREGK DEDKRDGNNE 101 DNEKLRKPKH KKLKQPGDGN PDPNANPNVD PNANPNVDPN ANPNVDPNAN \_\_\_\_\_ \_\_\_ \_\_\_ 

301 PNDPNRNVDE NANANNAVKN NNNEEPSDKH IEQYLKKIKN SISTEWSPCS 351 VTCGNGIQVR IKPGSANKPK DELDYENDIE KKICKMEKCS SVFNVVNSSI

401 GLIMVLSFLF LN

140-159, 204-223 HITS AT:

REFERENCE 1: 110:34817

REFERENCE 102:198973 2:

REFERENCE 3: 101:164640

FILE 'HOME' ENTERED AT 15:23:55 ON 06 DEC 2002

Shears 308-4994